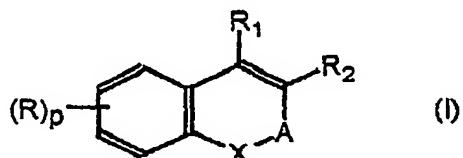


CLAIMS

1. The use of a pentadienoic acid derivative of formula (I) for the preparation of a medicament for the prevention or treatment of hyperuricemia and/or one or several associated disorders or diseases, and/or for reducing the serum uric acid level of a subject.

10



in which:

X represents O or S;

A represents either the divalent radical

15 $-(CH_2)_s-CO-(CH_2)_t-$ or the divalent radical $-(CH_2)_s-CR_3R_4-(CH_2)_t-$

in which radicals s = t = 0 or else one of s and t has the value 0 and the other has the value 1;

R₄ represents a hydrogen atom or a (C₁-C₁₅)alkyl group;

20 R₁ and R₂ independently represent the Z chain defined below; a hydrogen atom; a (C₁-C₁₈)alkyl group; a (C₂-C₁₈)alkenyl group; a (C₂-C₁₈)alkynyl group; a (C₆-C₁₀)aryl group optionally substituted by a halogen atom, by an optionally halogenated (C₁-C₅)alkyl group or by an 25 optionally halogenated (C₁-C₅)alkoxy group; or a mono- or bicyclic (C₄-C₁₂)heteroaryl group comprising one or more heteroatoms chosen from O, N and S which is optionally substituted by a halogen atom, by an optionally halogenated (C₁-C₅)alkyl group or by an optionally halogenated (C₁-C₅)alkoxy group;

30 R₃ and R₄ independently takes any one of the meanings given above for R₁ and R₂, with the exception of the Z chain; or else

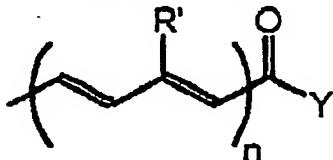
R_3 and R_4 together form a (C_2-C_6) alkylene chain optionally substituted by a halogen atom or by optionally halogenated (C_1-C_5) alkoxy;

R is chosen from a halogen atom; a cyano group; a 5 nitro group; a carboxy group; an optionally halogenated (C_1-C_{18}) alkoxy carbonyl group; an $R_a-CO-NH-$ or R_aR_bN-CO- group [in which R_a and R_b independently represent optionally halogenated (C_1-C_{18}) alkyl; a hydrogen atom; (C_6-C_{10}) aryl or (C_6-C_{10}) aryl (C_1-C_5) alkyl (where the aryl parts are optionally 10 substituted by a halogen atom, by an optionally halogenated (C_1-C_5) alkyl group or by an optionally halogenated (C_1-C_5) alkoxy group); (C_3-C_{12}) cycloalkyl optionally substituted by a halogen atom, by an optionally halogenated C_1-C_5 alkyl [sic] group or by an optionally halogenated (C_1-C_5) alkoxy 15 group]; an optionally halogenated (C_1-C_{18}) alkyl group; optionally halogenated (C_1-C_{18}) alkoxy; and (C_6-C_{10}) aryl, (C_6-C_{10}) aryl (C_1-C_5) alkyl, (C_6-C_{10}) aryloxy, (C_3-C_{12}) cycloalkyl, (C_3-C_{12}) cycloalkenyl, (C_3-C_{12}) cycloalkyloxy or (C_3-C_{12}) cycloalkenyloxy in which the aryl, cycloalkyl and 20 cycloalkenyl parts are optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5) alkyl or by optionally halogenated (C_1-C_5) alkoxy;

-OH;

p represents 0, 1, 2, 3 or 4;

25 Z represents the radical:



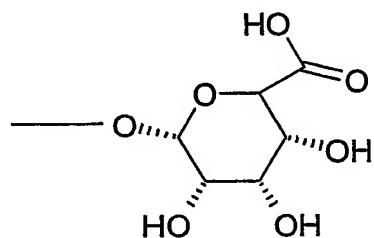
where n is 1 or 2;

the R' groups independently represent a hydrogen atom; a (C_1-C_5) alkyl group; a (C_6-C_{10}) aryl group optionally 30 substituted by a halogen atom, by an optionally halogenated (C_1-C_5) alkyl group or by optionally halogenated (C_1-C_5) alkoxy; or a mono- or bicyclic (C_4-C_{12}) heteroaryl group comprising one or more heteroatoms chosen from O, N and S which is optionally substituted by a halogen atom, by an

optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

Y represents -OH; (C_1-C_5)alkoxy; or the $-NR_cR_d$ group (in which R_c and R_d independently represent a hydrogen atom; (C_1-C_5)alkyl; (C_3-C_8)cycloalkyl optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy; (C_6-C_{10})aryl optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy;

10 Or Y represents glucomic acid



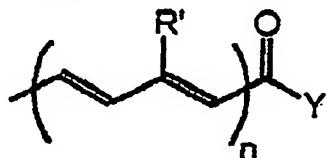
15 it being understood that one and one alone from R_1 and R_2 represents the Z chain;
 and their pharmaceutically acceptable salts with acids or bases, or esters.

20 2. The use according to Claim 1, characterized in that A represents the divalent radical $-(CH_2)_s- CR_3R_4- (CH_2)_t-$ in which s, t, R_3 and R_4 are as defined in Claim 1.

25 3. The use according to Claim 1, characterized in that:
 X represents O;
 A represents $-CR_3R_4-$ or $-CH_2-CR_3R_4-$ in which the unsubstituted methylene group is bonded to X;
 R_1 and R_2 independently represent Z; H; (C_1-C_{15})alkyl; (C_2-C_{15})alkenyl; or phenyl optionally substituted by (C_1-C_5)alkyl, (C_1-C_5)alkoxy, a halogen atom or $-CF_3$;
 30 R_3 and R_4 independently takes any one of the meanings given above for R_1 and R_2 , with the exception of Z;

R is chosen from (C₁-C₉)alkyl; (C₁-C₅)alkoxy; phenyl or phenylcarbonyl optionally substituted by a halogen atom, (C₁-C₅)alkyl, (C₁-C₅)alkoxy, -CF₃ or -OCF₃; a halogen atom; -CF₃ and -OCF₃;

5 Z represents the radical:



where n represents 1; and

R' represents (C₁-C₅)alkyl or (C₆-C₁₀)aryl.

10 4. The use according to any one of Claims 1 to 3, wherein :

X represents O;

A represents -CH₂-CR₃R₄- in which the unsubstituted methylene group is bonded to X;

15 R₁ and R₂ independently represent Z, a hydrogen atom or (C₁-C₅)alkyl;

R₃ and R₄ independently takes any one of the meanings given above for R₁ and R₂, with the exception of Z;

Z represents



20 R' represents methyl or phenyl.

5. The use according to anyone of claims 1 to 4, wherein R₁ represents Z.

25 6. The use according to anyone of claims 1 to 5, wherein R₂ represents a hydrogen atom.

7. The use according to anyone of claims 1 to 6, wherein Y is a (C₁-C₅) alkoxy.

30

8. The use according to any one of Claims 1 to 6, wherein :

Y represents -OH; (C₁-C₅)alkoxy; or -NR_cR_d in which R_c and R_d are as defined in Claim 1.

9. The use according to anyone of claims 1 to 8, wherein R' 5 is methyl.

10. The use according to any of claims 1 to 9, wherein R is (C₁-C₅) alkoxy.

10 11. The use according to any one of Claims 1 to 6, wherein p represents 0, 1 or 2.

12. The use according to claim 1, wherein :

[X represents O ;

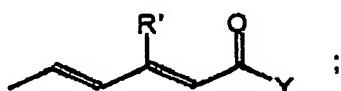
15 A represents -CH₂-CR₃R₄- in which the unsubstituted methylene group is bonded to X ;

R₁ is Z and R₂ is H;

R₃ and R₄ independently represents a (C₁-C₅) alkyl group;

20 R is a (C₁-C₅) alkoxy;

Z represents



wherein R' represents a methyl or phenyl ; and Y represents a (C₁-C₅) alkoxy].

25

13. The use according to claim 1 wherein said derivative is selected from the group consisting of

- (2E, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-30 2,4-dienoic acid;
- (2Z, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-6-methoxy-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;

- (2E, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- 5 - (2Z, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-[2-(non-6-enyl)-2H-1-benzopyran-3-yl]-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(4-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-10 2,4-dienoic acid;
- (2E, 4E)-5-(6-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(6-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- 15 - (2E, 4E)-5-(2-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(4-methyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- 20 - (2E, 4E)-5-(2-undecanyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(5-methyl-2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-2,4-dienoic acid;
- 25 - (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid; and
- (2E, 4E)-5-(2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-30 2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- 35 - (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

- (2E, 4E)-5-(3,3-dimethyl-7,8-dimethoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- 5 - (2E, 4E)-5-(3,3-dimethyl-2,3-dihydro-7-(para-chlorobenzoyl)benzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- 10 - (2E, 4E)-5-(3,3-dimethyl-7,8-dichloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-bromo-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- 15 - (2E, 4E)-5-(3,3-dimethyl-7-fluoro-8-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-fluoro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-trifluoromethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- 20 - (2E, 4E)-5-(3,3-dimethyl-7-phenyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3,7-trimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- 25 - (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(9-methoxy-3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

30 and their pharmaceutically acceptable esters.

14. The use according to anyone of claims 1 to 13 wherein the diseases associated with hyperuricemia to be treated comprise one or several of the following : gout, acute inflammatory arthritis, tophaceous deposition of urate crystals in and around joints, chronic arthritis, deposition of urate crystals in renal parenchyma,

urolithiasis, and related renal disease also termed gouty nephropathy.

15. The use according to anyone of claims 1 to 13 wherein
5 the hyperuricemiae to be treated comprises primary and
secondary hyperuricemiae, such as drug related to
hyperuricemiae (e.g. by diuretics, immunosuppressive or
cytotoxic agents), or hyperuricemiae related to diverse
medical conditions (e.g. nephropaties, myeloproliferative
10 disorders, conditions associated with insuline resistance
and transplantations).

16. The use according to any one of claims 1 to 13 to
prepare medicaments for subjects having serum uric acid
15 levels, before treatment, equal or above 7 mg/dL (420
µm/L).

17. The use according to claim 16 where the conditions to
be treated are gout or any condition brought about by high
20 levels of uric acid in the joints or kidneys or a serum
level over 9 mg/dL (530 µmol/L).

18. The use according to any of claims 1 to 17 for
preparing a medicament suitable for administering the 2,4-
25 pentadienoic acid derivative of formula (I) by the oral
route.

19. The use according to one of claims 1 to 18 for
preparing a medicament for administering the effective
30 amount of 2,4-pentadienoic acid or derivative according to
formula (I) once or twice per day.

20. The use according to any one of claims 1 to 19, wherein
the amount of said pentadienoic acid derivative is
35 substantially lower than the amount needed for the relevant
derivative as used in the treatment of dyslipidemia,
atherosclerosis and diabetes.

21. The use according to claim 20 wherein said amount is at least 50% lower.

22. The use according to claim 21 wherein said amount is at 5 least 90% lower.

23. The use according to any one of claims 1 to 20, wherein the amount of said pentadienoic acid derivative is from 0.15 to 4 mg/Kg of human body weight.

10

24. The use according to claim 23, wherein said amount is from 0.3 to 1.0 mg/Kg human body weight.

15

25. The use according to one of claims 1 to 24 wherein said derivative is (2E,4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzo-xepin-5-yl)-3-methylpenta-2,4-dienoic acid, or its pharmaceutically acceptable salts or esters, among which its ethyl ester.

20

26. New medical compositions for the treatment of hyperuricemiae and/or the above mentioned associated diseases or disorders and/or for reducing serum uric acid levels which comprise, in a vehicle acceptable for a human, an effective amount of at least one 2,4-pentadienoic acid derivative as defined in anyone of claims 1 to 13.

25

27. Medical compositions according to claim 26 wherein this effective amount is substantially lower than the amount needed for the relevant 2,4-pentadienoic acid derivative used in the treatment of dyslipidaemia, atherosclerosis and diabetes.

35

28. Medical compositions according to claim 27 wherein this effective amount is at least 50% lower.

29. Medical compositions according to claim 28 wherein this effective amount is at least 90% lower.

30. Medical compositions according to claim 26 wherein the effective amount in a dose for a one day administration for an adult is from 0.15 to 4 mg/kg of a human body.

5

31. Medical compositions according to anyone of claims 26 to 30, wherein said effective amount is from 0.3 to 1.0 mg/Kg of a human body.

10 32. Medical compositions according to anyone of claims 26 to 31 formulated for oral administration.

15 33. A medicament according to anyone of claims 26 to 32 wherein said derivative is (2E,4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzo-xepin-5-yl)-3-methylpenta-2,4-dienoic acid, or its pharmaceutically acceptable salts or esters, among which its ethyl ester.